

**AMENDMENTS**  
**In the Claims**

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MAR 10 2008

- 1.(canceled)
- 2.(canceled)
- 3.(canceled)
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- 6.(canceled)
- 7.(canceled)
- 8.(canceled)
- 9.(canceled)

1     10.(currently amended)     A composition comprising a polymerizing agent polymerase including  
2     a molecular tag covalently bonded to a site on the polymerizing agent polymerase and a monomer  
3     including nucleotide types for the polymerase, where at least one nucleotide type includes a  
4     molecular tag bonded to a part of the nucleotide that is released upon monomer nucleotide  
5     incorporation, where at least one of the tags has a fluorescence property that undergoes a change  
6     before, during and/or after each of a sequence of monomer nucleotide incorporations due to an  
7     interaction between the polymerizing agent polymerase and the monomer nucleotide and where the  
8     polymerizing agent polymerase lacks the ability to remove a previously incorporated monomer  
9     nucleotide.

- 11.(canceled)
- 12.(canceled)
- 13.(canceled)
- 14.(canceled)
- 15.(canceled)

1     16.(currently amended)     The composition of claim 10, wherein each of the monomers  
2     nucleotide types comprises a deoxynucleotide triphosphate (dNTP) and the monomer nucleotide tag  
3     is covalently bonded either directly or through a linker to the pyrophosphate moiety of each its  
4     dNTP.

1     17.(currently amended)     The composition of claim 10, wherein ~~the at least one tag~~ comprises  
2     ~~a fluorescent tag~~ and the fluorescence property comprises a duration, an intensity and/or frequency  
3     of emitted fluorescent light.

1     18.(currently amended)     The composition of claim ~~17~~10, wherein the polymerase tag comprises

2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer  
3 (FRET), where either the monomer nucleotide tag or the polymerase tag comprises a donor and the  
4 other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

1 19.(currently amended) The composition of claim ~~13~~108, wherein the polymerase comprises  
2 *Taq* DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of  
3 the *Taq* DNA polymerase I, where the amino acid position and the site is or the sites are selected  
4 from the group consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, where the tag  
5 comprises a fluorescent molecule.

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45.(canceled)

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49.(canceled)

1 50.(currently amended) A composition comprising a polymerizing agent polymerase including

2 a molecular tag covalently bonded to a site on the ~~polymerizing agent~~ polymerase and a  
3 deoxynucleotide triphosphate (dNTP) types for the polymerase, where at least one dNTP type  
4 including includes a molecular tag covalently bonded directly or through a linker to the  
5 pyrophosphate moiety a part of the dNTP the is release upon dNTP incorporation, where at least one  
6 of the tags has a fluorescence property that undergoes a change before, during and/or after each of  
7 a sequence of monomer dNTP incorporations due to an interaction between the ~~polymerizing agent~~  
8 polymerase and the dNTP.

1 51.(currently amended) The composition of claim 50, wherein the ~~polymerizing agent~~  
2 polymerase is a polymerase or reverse transcriptase.

1 52.(currently amended) The composition of claim ~~51~~50, wherein the polymerase is selected  
2 from the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the  
3 Klenow fragment from *E. coli* DNA polymerase I.

1 53.(previously presented) The composition of claim 51, wherein the reverse transcriptase  
2 comprises HIV-1 reverse transcriptase.

1 54.(currently amended) The composition of claim 50, wherein ~~at least one of the tags~~  
2 ~~comprises a fluorescent tag and the fluorescence property comprises a duration, an intensity and/or~~  
3 ~~frequency of emitted fluorescent light.~~

1 55.(currently amended) The composition of claim ~~54~~50, wherein the polymerase tag comprises  
2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer  
3 (FRET), where either the monomer nucleotide tag or the polymerase tag comprises a donor and the  
4 other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

5 56.(previously presented) The composition of claim ~~52~~109, wherein the polymerase comprises  
6 *Taq* DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of  
7 ~~the *Taq* DNA polymerase I, where the amino acid position and the site is or the sites are~~ selected  
8 from the group consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, ~~where the tag~~  
9 ~~comprises a fluorescent molecule.~~

57.(canceled)

58.(canceled)

59.(canceled)

60.(canceled)

61.(canceled)

62.(canceled)

63.(canceled)

1 64.(currently amended) A composition comprising a ~~polymerizing agent~~ polymerase including  
2 a molecular tag covalently bonded to a site on the ~~polymerizing agent~~ polymerase and a  
3 deoxynucleotide triphosphate (dNTP) types for the polymerase, where at least one dNTP type  
4 including includes a molecular tag covalently bonded directly or through a linker to the  $\gamma$  phosphate  
5 group of the dNTP, where at least one of the tags has a fluorescence property that undergoes a  
6 change before, during and/or after each of a sequence of ~~monomer~~ dNTP incorporations due to an  
7 interaction between the ~~polymerizing agent~~ polymerase and the dNTP.

1 65.(currently amended) The composition of claim 64, wherein the ~~polymerizing agent is a~~  
2 polymerase or comprises a reverse transcriptase.

1 66.(currently amended) The composition of claim ~~65~~64, wherein the polymerase is selected  
2 from the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the  
3 Klenow fragment from *E. coli* DNA polymerase I.

1 67.(previously presented) The composition of claim 65, wherein the reverse transcriptase  
2 comprises HIV-1 reverse transcriptase.

1 68.(currently amended) The composition of claim 64, wherein ~~at least one of the tags~~  
2 ~~comprises a fluorescent tag and the fluorescence property comprises a duration, an intensity and/or~~  
3 frequency of emitted fluorescent light.

1 69.(currently amended) The composition of claim ~~68~~64, wherein the polymerase tag comprises  
2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer  
3 (FRET), where either the ~~monomer~~ nucleotide tag or the polymerase tag comprises a donor and the  
4 other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

5 70.(currently amended) The composition of claim ~~66110~~, wherein the polymerase comprises  
6 *Taq* DNA polymerase I ~~having a tag attached to an amino acid at a specific amino acid position of~~  
7 ~~the *Taq* DNA polymerase I, where the amino acid position and the site is or the sites are selected~~  
8 ~~from the group consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11; where the tag~~  
9 ~~comprises a fluorescent molecule.~~

1 71.(currently amended) A composition comprising a polymerizing agent polymerase including  
2 a molecular tag covalently bonded to a site on the polymerizing agent polymerase and a monomer  
3 including nucleotide types for the polymerase, where at least one nucleotide type includes a  
4 molecular tag covalently bonded directly or through a linker to the terminal phosphate of the  
5 monomer nucleotide, where at least one of the tags has a fluorescence property that undergoes a  
6 change before, during and/or after each of a sequence of monomer nucleotide incorporations due  
7 to an interaction between the polymerizing agent polymerase and the monomer nucleotide.

1 72.(currently amended) The composition of claim 71, wherein the ~~polymerizing agent is a~~  
2 ~~polymerase or~~ comprises a reverse transcriptase.

1 73.(currently amended) The composition of claim ~~7271~~, wherein the polymerase is selected  
2 from the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the  
3 Klenow fragment from *E. coli* DNA polymerase I.

1 74.(previously presented) The composition of claim 72, wherein the reverse transcriptase  
2 comprises HIV-1 reverse transcriptase.

75.(canceled)

1 76.(currently amended) The composition of claim 71, wherein ~~at least one of the tags~~  
2 ~~comprises a fluorescent tag and the fluorescence property comprises a duration, an intensity and/or~~  
3 ~~frequency of emitted fluorescent light.~~

1 77.(currently amended) The composition of claim ~~7671~~, wherein the polymerase tag comprises  
2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer  
3 (FRET), where either the monomer nucleotide tag or the polymerase tag comprises a donor and the

other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

78.(currently amended) The composition of claim 73~~111~~, wherein the polymerase comprises *Taq* DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the *Taq* DNA polymerase I, where the amino acid position and the site is or sites are selected from the group consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11, where the tag comprises a fluorescent molecule.

79.(currently amended) A composition comprising a ~~polymerizing agent~~ polymerase including a molecular tag covalently bonded to a site on the ~~polymerizing agent~~ polymerase lacking 3' to 5' exonuclease activity and a ~~monomer including nucleotide types for the polymerase, where at least one nucleotide type includes~~ a molecular tag bonded to a part of the nucleotide that is released upon ~~monomer nucleotide~~ incorporation, where at least one of the tags has a fluorescence property that undergoes a change before, during and/or after each of a sequence of ~~monomer nucleotide~~ incorporations due to an interaction between the ~~polymerizing agent~~ polymerase tag and the ~~monomer nucleotide~~ tag and where the site comprises a naturally occurring cysteine site or a cysteine replacement site in the ~~polymerizing agent~~ polymerase selected so that the site is less than or equal to about 50Å from a tag on each incorporating ~~monomer nucleotide~~ and is a site that is not involved in the function of the ~~polymerizing agent~~ polymerase and the ~~polymerizing agent~~ polymerase tag is covalently bonded to the naturally occurring cysteine site or the cysteine replacement site through its SH group.

80.(currently amended) The composition of claim 79, wherein the site is less than or equal to about 15Å from a tag on each incorporating ~~monomer nucleotide~~.

81.(currently amended) The composition of claim 79, wherein the site is less than or equal to about 10Å from a tag on each incorporating ~~monomer nucleotide~~.

82.(currently amended) The composition of claim 79, wherein the ~~polymerizing agent~~ is a polymerase or comprises a reverse transcriptase.

83.(previously presented) The composition of claim 79, wherein the polymerase is selected from

2 the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the Klenow  
3 fragment from *E. coli* DNA polymerase I.

1 84.(previously presented) The composition of claim 82, wherein the reverse transcriptase  
2 comprises HIV-1 reverse transcriptase.

1 85.(currently amended) The composition of claim 79, wherein each of the monomers  
2 nucleotides comprises a deoxynucleotide triphosphate (dNTP) and the monomer nucleotide tag is  
3 covalently bonded directly or through a linker to the pyrophosphate moiety of each its dNTP.

1 86.(currently amended) The composition of claim ~~85~~79, wherein the tag ~~comprise~~ fluorescent  
2 tag and the fluorescence property comprises a duration, an intensity and/or frequency of emitted  
3 fluorescent light.

1 87.(currently amended) The composition of claim ~~86~~79, wherein the polymerase tag comprises  
2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer  
3 (FRET), where either the monomer nucleotide tag or the polymerase tag comprises a donor and the  
4 other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

5 88.(currently amended) The composition of claim 83, wherein the polymerase comprises *Taq*  
6 DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the  
7 ~~*Taq* DNA polymerase I, where the amino acid position and the site is selected from the group~~  
8 ~~consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11; where the tag comprises a~~  
9 ~~fluorescent molecule.~~

1 89.(currently amended) A composition comprising a polymerizing agent polymerase including  
2 a molecular tag covalently bonded to a site on the polymerizing agent polymerase and a monomer  
3 nucleotide including a molecular tag covalently bonded to the monomer and a part of the nucleotide  
4 that is released upon monomer nucleotide incorporation, where at least one of the tags has a  
5 fluorescence property that undergoes a change before, during and/or after each of a sequence of  
6 monomer nucleotide incorporations due to an interaction between the polymerizing agent  
7 polymerase tag and the monomer nucleotide tag and where the site comprises a naturally occurring

8 cysteine site or a cysteine replacement site in the ~~polymerizing agent~~ polymerase selected so that  
9 the site is less than or equal to about 50Å from a tag on each incorporating monomer nucleotide and  
10 the ~~polymerizing agent~~ polymerase tag is covalently bonded to the naturally occurring cysteine site  
11 or the cysteine replacement site through its SH group.

1 90.(currently amended) The composition of claim 89, wherein the site is less than or equal to  
2 about 15Å from a tag on each incorporating monomer nucleotide .

1 91.(currently amended) The composition of claim 89, wherein the site is less than or equal to  
2 about 10Å from a tag on each incorporating monomer nucleotide .

1 92.(currently amended) The composition of claim 89, wherein the ~~polymerizing agent is a~~  
2 polymerase or comprises a reverse transcriptase.

1 93.(canceled)

1 94.(currently amended) The composition of claim ~~9289~~, wherein the polymerase is selected  
2 from the group consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the  
3 Klenow fragment from *E. coli* DNA polymerase I.

1 95.(previously presented) The composition of claim 92, wherein the reverse transcriptase  
2 comprises HIV-1 reverse transcriptase.

1 96.(currently amended) The composition of claim 89, wherein each of the monomers  
2 nucleotides comprises a deoxynucleotide triphosphate (dNTP) and the monomer nucleotide tag is  
3 covalently bonded directly or through a linker to the terminal phosphate group of each its dNTP.

1 97.(currently amended) The composition of claim ~~9689~~, wherein ~~the tags comprise fluorescent~~  
2 ~~tags and~~ the fluorescence property comprises a duration, an intensity and/or frequency of emitted  
3 fluorescent light.

1 98.(currently amended) The composition of claim 97, wherein the polymerase tag comprises  
2 a fluorescent tag and wherein the fluorescence property is fluorescence resonance energy transfer



3 (FRET), where either the monomer nucleotide tag or the polymerase tag comprises a donor and the  
4 other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

5 99.(previously presented) The composition of claim 94, wherein the polymerase comprises *Taq*  
6 DNA polymerase I having a tag attached to an amino acid at a specific amino acid position of the  
7 ~~*Taq* DNA polymerase I, where the amino acid position and the site~~ is selected from the group  
8 consisting of 513-518, 643, 647, 649 and 653-661 of SEQ. ID No. 11; ~~where the tag comprises a~~  
9 ~~fluorescent molecule.~~

1 100.(previously presented) The composition of claim 50, wherein the polymerizing agent lacks  
2 the ability to remove a previously incorporated monomer nucleotide.

101.(canceled)

1 102.(previously presented) The composition of claim 64, wherein the polymerase is free of or  
2 lacks the ability to remove a previously incorporated monomer nucleotide.

1 103.(previously presented) The composition of claim 71, wherein the polymerase is free of or  
2 lacks the ability to remove a previously incorporated monomer nucleotide.

1 104.(previously presented) The composition of claim 89, wherein the polymerase is free of or  
2 lacks the ability to remove a previously incorporated monomer nucleotide.

1 105.(previously presented) The composition of claim 79, wherein the site is less than or equal to  
2 about 25Å from a tag on each incorporating monomer nucleotide.

1 106.(previously presented) The composition of claim 89, wherein the site is less than or equal to  
2 about 25Å from a tag on each incorporating monomer nucleotide.

107.(canceled)

1 108.(new) The composition of claim 10, wherein the polymerase comprises a genetically  
2 engineered polymerase comprising a native polymerase including one cysteine residue replacement  
3 or a plurality of cysteine residue replacements at one site or a plurality of sites of the native

4 polymerase, where the site or sites are not in contact with other proteins, where the site or sites do  
5 not alter the conformation or folding of the polymerase, where the site or sites are not involved in  
6 the functioning of the polymerase, and where the polymerase tag is bonded to the polymerase  
7 through a cysteine residue replacement or through a plurality of cysteine residue replacements.

1 109.(new) The composition of claim 50, wherein the polymerase comprises a genetically  
2 engineered polymerase comprising a native polymerase including one cysteine residue replacement  
3 or a plurality of cysteine residue replacements at one site or a plurality of sites of the native  
4 polymerase, where the site or sites are not in contact with other proteins, where the site or sites do  
5 not alter the conformation or folding of the polymerase, where the site or sites are not involved in  
6 the functioning of the polymerase, and where the polymerase tag is bonded to the polymerase  
7 through a cysteine residue replacement or through a plurality of cysteine residue replacements.

1 110.(new) The composition of claim 64, wherein the polymerase comprises a genetically  
2 engineered polymerase comprising a native polymerase including one cysteine residue replacement  
3 or a plurality of cysteine residue replacements at one site or a plurality of sites of the native  
4 polymerase, where the site or sites are not in contact with other proteins, where the site or sites do  
5 not alter the conformation or folding of the polymerase, where the site or sites are not involved in  
6 the functioning of the polymerase, and where the polymerase tag is bonded to the polymerase  
7 through a cysteine residue replacement or through a plurality of cysteine residue replacements.

1 111.(new) The composition of claim 71, wherein the polymerase comprises a genetically  
2 engineered polymerase comprising a native polymerase including one cysteine residue replacement  
3 or a plurality of cysteine residue replacements at one site or a plurality of sites of the native  
4 polymerase, where the site or sites are not in contact with other proteins, where the site or sites do  
5 not alter the conformation or folding of the polymerase, where the site or sites are not involved in  
6 the functioning of the polymerase, and where the polymerase tag is bonded to the polymerase  
7 through a cysteine residue replacement or through a plurality of cysteine residue replacements.